toxicities (H-tox and NH-tox) at 4 months and grade 2−4 neurological at 6 months were the endpoints of the study. Thirteen genetic variants in 10 candidate genes were selected for pharmacogenetic analysis: ERCC1_04 (rs3212961), ERCC1_05 (rs11615), ERCC1_06 (rs3212948), ERCC1_24 (rs3212955), ERCC2_02 (rs1799793), ERCC2_03 (rs13181), ERCC2_06 (rs238406), ERCC2_09 (rs1799787), GSTM1 (null/present), GSTT1 (null/present), TS (TSER, Ins/del6bp) and UGT1A1 (rs8175347). Genotyping was performed using Taqman probes, QMPSF and fragment analysis.
Results: 327 pts (156/171) out of 410 were included (61 had no blood samples, 16 had less than 2 cycles, 3 had incomplete data on toxicity, 3 had insufficient DNA). No difference was found between included and excluded pts in the analysis for gender, age, OMS, number of metastatic organs and adjuvant chemotherapy. Pts received similar 5FU doses in both arms. Number of patients with at least one toxicity in arms 1/2 were as follows: 5/54 grade 3−4 H-tox, 28/47 grade 3−4 NH-tox, and 0/103 grade 2−4 neurological. The genotype CC of ERCC2_02 correlated with higher NH-tox at 4 months in arm 2 ($p = 0.0008$, OR = 0.31, 95% CI=[0.15−0.62] versus $p = 0.87$, OR = 0.93, CI=[0.39−2.21] in arm 1) compared to genotypes CT and TT, with borderline interaction ($p = 0.05$).
Conclusions: These preliminary results on early toxicity in first-line are in favour of an effect of ERCC2_02 on NH-tox of FOLFOX6 and a predictive effect on NH-tox of oxaliplatin.

3019 POSTER

Association of gene copy number (GCN) of the epidermal growth factor receptor (EGFr) and clinical outcome in patients (pts) with metastatic colorectal cancer (mCRC) treated with panitumumab monotherapy

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Background: Panitumumab, a fully human monoclonal antibody directed against EGFr, has demonstrated efficacy as monotherapy in pts with mCRC. Recently, differences with regards to the predictive value of EGFr GCN with response to anti-EGFr therapy have been published. In this analysis, we associate clinical outcome with EGFr GCN from pt samples from a large, phase 2 panitumumab monotherapy study of mCRC.
Methods: Tumor sections from 39/148 treated pts who were consented, had response data, and were available for testing were included in this analysis. EGFr GCN was analyzed by FISH using the Vysis® kit (per the kit protocol; Des Plaines, IL). Increased GCN (# EGFr signals per nucleus) was defined as >2.5, and amplification (EGFr signals/CEP7 signals) was defined as >1.1. Best objective response (OR) was assessed using modified RECIST criteria at prespecified weeks by blinded central review. Association of EGFR GCN with clinical outcomes was tested using a Fisher's Exact Test for best OR, and a Cox Proportional Hazards model for progression-free survival (PFS) and overall survival (OS).

	PR	SD	PD
GCN > 2.5	0/5	4/13	5/18
Rate[a]	0%	31%	28%
p-value		0.51	
Amplification >1.1	0/5	6/13	2/18
Rate[a]	0%	46%	11%
p-value	0.05		
GCN (continuous)	**PFS**	**OS**	
HR[b]	1.00	1.00	
95% CI	0.83−1.21	0.82−1.21	
Amplification (continuous)			
HR[b]	0.87	0.93	
95% CI	0.37−2.04	0.42−2.08	

[a]Fisher's exact test; [b]CoxPH model.

Results: 36/39 pt samples were evaluable by FISH and were included in this analysis. Five (14%) pts had a partial response (PR), 13 (36%) pts had stable disease (SD), and 18 (50%) had progressive disease (PD). Analyses by clinical efficacy outcomes are shown (table). Additional analyses on FISH using ROC curves for parameters of response, survival and PFS were negative. Similar results were obtained with gene amplification. Based on these results, we would be unable to ascribe any value to GCN or gene amplification as an indicator of outcome.
Conclusion: In this data set, EGFr GCN and gene amplification do not predict response (PR, SD, or PD), OS or PFS with panitumumab. These findings warrant further investigation in a larger set of samples.

3020 POSTER

Preliminary efficacy of Bevacizumab with first-line Folfox, Xelox, Folfiri and fluoropyrimidines for mCRC: First BEAT trial

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Background: In a phase III pivotal trial in patients (pts) with metastatic colorectal cancer (mCRC), BEV (BEV, Avastin®) increased overall survival (OS) by 30% when added to first-line IFL chemotherapy (CT). Recently, a second trial reported a significant improvement in progression free survival (PFS) when BEV was added to FOLFOX/XELOX in a similar patient population. Although, First BEAT was opened to evaluate the safety profile of BEV in a broader pt population using a variety of CT regimens, efficacy endpoints were investigated.
Material and Methods: First BEAT screened 1,965 mCRC patients in 41 countries between June 2004 and February 2006. 1,914 eligible pts were treated with first-line CT (physician's choice) in combination with BEV (5 mg/kg q2w [5-FU-based CT] or 7.5 mg/kg q3w [capecitabine [cap, Xeloda®]-based CT]) until disease progression. Secondary endpoints included OS, time to progression (TTP) and PFS. Disease progression was assessed by investigators. A confirmatory analysis censored pts who discontinued Bev before progression.
Results: All eligible pts were evaluable by 16 March 2007 (male 58%; median age 59 years, 33% ⩾65 years; ECOG PS 0/1 65%/34%). Median follow-up was 18 months; 60-day mortality was 2.5%. First-line CT regimens used with BEV included FOLFOX (28%), FOLFIRI (26%), XELOX (18%) and 5-FU /cap monotherapy (15%). 55% of pts were treated until progression. Pts receiving 5 FU/cap CT appeared to have poorer prognosis with respect to age ⩾65 years (41%), ECOG PS 0/1 (58%/42%) and 60-day mortality rate (6.6%), compared with those receiving doublet CT regimens plus BEV. Median overall PFS was 10.7 (95% CI: 10.3−11.2 months, based on 1,110 events), 10.6 (9.8−12.0) in FOLFOX, 10.7 (10.1−11.6) in XELOX, 11.3 (10.7−12.4) in FOLFIRI and 9.1 (8.1−10.3) in pts receiving 5-FU or cap CT with BEV, respectively. Median overall TTP was 11.1 (95% CI: 10.6−11.6) months (based on 1,026 events). On treatment median PFS was 11.2 (95% CI: 10.7−11.7 months) and TTP was 11.5 (95% CI: 11.0−12.3 months). Metastasectomy was performed in 143 (7.5%) pts, of which 85% were done with curative intent. 614 pts have died, but OS data are immature. Updated analyses will be presented.
Conclusions: In this ongoing, large community-based study, the preliminary efficacy of first line BEV in mCRC pts receiving a variety of CT regimens appears consistent with that observed in large phase III randomised trials.

3021 POSTER

Association between exposure to bevacizumab (BV) beyond first progression (BBP) and overall survival (OS) in patients (pts) with metastatic colorectal cancer (mCRC): results from a large observational study (BRiTE)

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Background: While BV (Avastin®) prolongs OS when used with standard 1st- or 2nd-line chemotherapy (CT) in mCRC, no data exist on the effects of BBP. A previous report from BRiTE showed favorable median OS (27.1 mo, 95% CI 24.8-NE), with 1st line PFS (median 10.1 mo, 95% CI:9.7−10.4)